A 52-Week Multicenter, Randomized, Open-Label, Parallel-Group Study Evaluating the Efficacy and Safety of Ixekizumab versus Adalimumab in Patients with Psoriatic Arthritis Who Are Biologic Disease-Modifying Anti-Rheumatic Drug Naive

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Primary objective:-To assess whether ixekizumab is superior to adalimumab at Week 24 in the treatment of patients with active PsA as measured by American Collegeof Rheumatology 50 (ACR50) and Psoriasis Area and Severity Index 100 (PASI 100)Major...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Joint disorders
Study type	Interventional

Summary

ID

NL-OMON45393

Source
ToetsingOnline

Brief title
I1F-MC-RHCF

Condition

- Joint disorders

Synonym
disease causing swollen and painful joints, Psoriatic arthritis

Research involving
Human

Sponsors and support

Primary sponsor: Eli Lilly
Source(s) of monetary or material Support: Eli Lilly

Intervention

Keyword: Ixekizumab, Multicenter, Phase 3, Psoriatic Arthritis

Outcome measures

Primary outcome

-Proportion of patients simultaneously achieving ACR50 and PASI 100 at Week 24

Secondary outcome

-Proportion of patients achieving ACR50 in each treatment group at Week 24

-Proportion of patients achieving PASI 100 in each treatment group at Week 24

PsA Endpoints

Time course of response to treatment over 52 weeks as measured by:

-Proportion of patients achieving ACR20, ACR50, and ACR70 responses

-Change from baseline in individual components of the American College of Rheumatology (ACR) Core Set - tender joint count, swollen joint count, patient*s pain assessment, Patient*s Global Assessment of Disease Activity, Physician*s Global Assessment of Disease Activity, C-reactive protein (CRP), and Health Assessment Questionnaire*Disability Index (HAQ-DI) score

-Proportion of patients simultaneously achieving ACR50 and PASI 100 response

-Change from baseline in the Disease Activity Score (28 diarthrodial joint count) based on C-reactive protein (DAS28-CRP)

-Proportion of patients achieving Minimal Disease Activity (MDA)

-Proportion of patients achieving Psoriatic Arthritis Response Criteria (PsARC)

-Change from baseline in Modified Composite Psoriatic Disease Activity Index (CPDAI) score

-Proportion of patients achieving low disease activity or remission according to the Modified Composite Psoriatic Disease Activity Index definition

-Proportion of patients with HAQ-DI improvement *0.35

-Change from baseline in the Spondyloarthritis Research Consortium of Canada (SPARCC) Enthesitis Index score in patients with enthesitis at baseline (ie, baseline SPARCC Enthesitis Index score >0)

-Change from baseline in the Leeds Enthesitis Index (LEI) score in patients with enthesitis at baseline (ie, baseline LEI score >0)

-Proportion of patients with resolution in enthesitis in the subgroup of patients with enthesitis at baseline as measured by the SPARCC Enthesitis Index (ie, baseline SPARCC Enthesitis Index score >0)

-Proportion of patients with resolution in enthesitis in the subgroup of patients with enthesitis at baseline as measured by the LEI (ie, baseline LEI score >0)

-Change from baseline in the Leeds Dactylitis Index-Basic (LDI-B) score in patients with dactylitis at baseline (ie, baseline LDI-B score >0)

-Proportion of patients with resolution in dactylitis in the subgroup of patients with dactylitis at baseline as measured by the LDI-B (ie, baseline LDI-B score >0)

Psoriasis/Nail Endpoints

Time course of response to treatment over 52 weeks as measured by:

-Change from baseline in body surface area (BSA)

-Proportion of patients who achieve the following PASI scores: PASI 75, PASI 90, or PASI 100 (defined as 75%, 90%, and 100% improvement from baseline in PASI criteria, respectively)

-Proportion of patients achieving an absolute PASI score <1 or <2 or <3

-Change from baseline in the Nail Psoriasis Severity Index (NAPSI) Fingernails score in the subgroup of patients with fingernail involvement at baseline (ie, baseline NAPSI Fingernails score >0)

QoL Endpoints

Time course of response to treatment over 52 weeks as measured by:

-Change from baseline in the Itch Numeric Rating Scale (NRS) score

-Proportion of patients with Itch NRS score equal to 0

-Change from baseline in Fatigue Severity NRS score

-Change from baseline in Medical Outcomes Study 36-Item Short Form Health Survey (SF-36)

o Physical Component Summary score

o Mental Component Summary score

-Change from baseline in measures of health utility (European Quality of Life*5 Dimensions 5 Level health outcomes instrument [EQ-5D-5L])

-Change from baseline in Dermatology Life Quality Index (DLQI) total score

-Change from baseline in Treatment Satisfaction Questionnaire Safety

-Change from baseline in Columbia*Suicide Severity Rating Scale (C-SSRS)

Study description

Background summary

During the last decade, the treatment of psoriatic arthritis (PsA) has significantly changed. Methotrexate (MTX) or other conventional synthetic disease-modifying anti-rheumatic drugs (csDMARD) such as sulfasalazine or leflunomide are usually initiated as a first line of treatment.
In patients with active PsA and an inadequate response or intolerance to a csDMARD, the use of a biologic DMARD (bDMARD) is recommended according to the European League Against Rheumatism (EULAR) and Group for Research and Assessment of Psoriasis and Psoriatic
Arthritis (GRAPPA) working group.
Based on current treatment recommendations, a tumor necrosis factor (TNF) inhibitor is the usual first option for a bDMARD, mainly because of the long-term experience and the well-established efficacy and safety profile of these agents. Five TNF inhibitors have been approved and are available in major markets for the treatment of PsA to-date: etanercept, infliximab, adalimumab, golimumab, and certolizumab. In addition, biosimilars of infliximab, etanercept, and adalimumab have been recently approved for use in PsA. New bDMARDs targeting different mechanisms of action have also been approved for the treatment of PsA, with ustekinumab targeting the IL-12/IL-23 pathway, secukinumab and brodalumab targeting the IL-17 pathway, and apremilast, an oral molecule, inhibiting phosphodiesterase 4 (PDE 4). As additional therapies become available, an important question is whether bDMARDs with different mechanisms of action have comparable clinical efficacy and safety. Ixekizumab has been studied in patients with active PsA in a study that included adalimumab as an active control reference arm. Yet to date, no results of a direct comparator study in patients with PsA comparing 2 bDMARDs have been published. This type of study design is important for informing evidence-based treatment decisions with regard to a TNF inhibitor.
In this study, adalimumab has been chosen as the active comparator, as it is recognized as a standard of care for a bDMARD in the treatment of active PsA.

Study objective

Primary objective:
-To assess whether ixekizumab is superior to adalimumab at Week 24 in the treatment of patients with active PsA as measured by American College of Rheumatology 50 (ACR50) and Psoriasis Area and Severity Index 100 (PASI 100)

Major Secondary Objectives:

-To assess whether ixekizumab is noninferior to adalimumab at Week 24 in the treatment of patients with active PsA as measured by ACR50
-To assess whether ixekizumab is superior to adalimumab at Week 24 in the treatment of patients with active PsA as measured by PASI 100

Other Secondary Objectives:
-To assess the effect of treatment with ixekizumab compared with adalimumab as measured by efficacy and quality of life outcomes

Study design

Study RHCF is a Phase 3b/4, multicenter, randomized, open-label, parallel-group study with blinded outcomes assessments evaluating the efficacy and safety of ixekizumab versus adalimumab in patients with PsA who are bDMARD naive during a 52-week treatment period.

The study will consist of 3 periods:
- Period 1: Screening Period (Visit 1) up to 28 days before randomization (Visit 2)
- Period 2: Open-Label Treatment Period (Visit 2 through Visit 11) from Week 0 to Week 52
- Period 3: Post-Treatment Follow-Up Period occurring from last treatment visit during Period 2 or Early Termination Visit (ETV) up to a minimum of 12 weeks after that visit

Intervention

At Week 0 (randomization, Visit 2), routine safety assessments, laboratory tests, and clinical efficacy assessments (including height, weight, and temperature, as well as review of habits) will be performed on eligible patients according to the Schedule of Activities (Protocol section 2). Patients will be randomized at a 1:1 ratio to either ixekizumab 80 mg or adalimumab 40 mg.

The study will consist of 3 periods:
- Period 1: Screening Period (Visit 1) up to 28 days before randomization (Visit 2)
- Period 2: Open-Label Treatment Period (Visit 2 through Visit 11) from Week 0 to Week 52
- Period 3: Post-Treatment Follow-Up Period occurring from last treatment visit during Period 2 or Early Termination Visit (ETV) up to a minimum of 12 weeks after that visit

All patients randomized to ixekizumab will receive a starting dose of 160 mg at randomization (Visit 2 [Week 0]). Patients with moderate-to-severe plaque Ps will receive ixekizumab 80 mg Q2W from Week 2 to Week 12 and Q4W thereafter.

Patients not meeting criteria for moderate-to-severe plaque Ps at randomization will receive ixekizumab 80 mg Q4W starting at Week 4.

Patients randomized to adalimumab with moderate-to-severe plaque Ps will receive a starting dose of 80 mg at randomization (Visit 2 [Week 0]) followed by 40 mg Q2W starting at Week 1.
Patients not meeting criteria for moderate-to-severe plaque Ps will receive a starting dose of 40 mg at randomization (Visit 2) followed by 40 mg Q2W starting at Week 2 (see Protocol section 7.1 for details regarding treatments administered).

Study burden and risks

The Investigational Product and other medication required by Protocol and the study procedures are associated with certain risks and discomforts, as described in the patient information leaflet. The combination of experimental medicine and study procedures may be associated with additional risks or discomforts that at this point are not fully known. The most common side effects associated with lxekizumab are: Runny nose and sore throat; cold symptoms; Upper respiratory tract infection; injection site reaction; Headache; Worsening of rheumatoid arthritis; Urinary tract Infection; Sinus irritation; Injection site pain; Injection site redness; Diarrhea; Back pain; Bronchitis; High blood pressure; Dizziness; Joint pain; Cough; Nausea; Vertigo.
The subjects undergo an number of study procedures such as SC injections, TB test and X-ray. These procedures may also be accompanied by certain risks. The procedures may also have other unknown risks. These risks are described in the Informed consent form. Selectively targeting IL-17A with ixekizumab is hypothesized to provide therapeutic benefit without unduly impacting host defenses. As such, ixekizumab may offer a therapeutic option for patients who have failed NSAIDs and for patients who have lost response, failed to respond, or are intolerant to current marketed drugs. Ixekizumab may offer a more favorable safety profile compared to currently marketed therapies.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

-Presents with established diagnosis of active psoriatic arthritis for at least 6 months, and currently meets Classification for Psoriatic Arthritis (CASPAR) criteria
-Active psoriatic arthritis (PsA) defined as the presence of at least 3 tender and at least 3 swollen joints
-Presence of active plaque psoriasis
-Men must agree to use a reliable method of birth control or remain abstinent during the study
-Women must agree to use reliable birth control or remain abstinent during the study and for at least 12 weeks after stopping treatment

Exclusion criteria

-Current or prior use of biologic agents for treatment of Ps or PsA
-Evidence of active inflammatory arthritic syndromes or spondyloarthropathies other than PsA
-Have participated in any study with interleukin 17 (IL-17) antagonists, including ixekizumab
-Serious disorder or illness other than psoriatic arthritis
-Serious infection within the last 3 months
-Women who are breastfeeding

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	30-01-2018
Enrollment:	4
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Humira
Generic name:	Adalimumab
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Taltz
Generic name:	Ixekizumab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	25-04-2017
Application type:	First submission

Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	04-07-2017
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	04-08-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	06-12-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	11-12-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	05-03-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	06-03-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	11-02-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	18-02-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	05-08-2019
Application type:	Amendment

Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	12-08-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2016-004585-25-NL
CCMO	NL61357.048.17